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The Next Flu Pandemic: Evaluating U.S. Preparedness

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Mr. Chairman and members of the Subcommittee, I am pleased to be here today to describe planning and preparedness for an influenza pandemic, including the potential threat posed by the H5N1 avian influenza virus currently circulating in Asia. Department of Health and Human Services (DHHS) Secretary Mike Leavitt has made influenza pandemic planning and preparedness a top priority. Agencies within DHHS are working together formally through the Influenza Preparedness Task Force that Secretary Leavitt has chartered to prepare the United States for this potential threat to the health of our nation.

I will discuss steps the Centers for Disease Control and Prevention (CDC) is taking as a member of this Task Force and with many other partners both domestically and globally. The strength and flexibility of CDC and other components of the public health system are vital assets as the U.S. sharpens its readiness for an influenza pandemic. Although we have made significant progress, more work is needed, particularly in the areas of surveillance capacity and response, and in the development of potential vaccines. Increased public awareness and understanding about infection control, community containment and travel, and other actions also are important in preparation for an influenza pandemic.

In discussing pandemic influenza, I want to emphasize that the issues of pandemic influenza and inter-pandemic influenza (so-called “annual influenza”) are inextricably linked. The same laboratories, the same health care providers,

the same surveillance systems, and the same health department plans and personnel will guide both responses. Making sure that these people and organizations can address inter-pandemic influenza is our best overall hope for making sure the U.S. is prepared for an influenza pandemic.

Pandemics in Perspective

Inter-pandemic influenza causes an average of 36,000 deaths each year in the U.S., mostly among the elderly and nearly 200,000 hospitalizations. In contrast, the severity and impact of the next pandemic, whether from H5N1 or another influenza virus, cannot be predicted. However, modeling studies suggest that, in the absence of any control measures, a "medium-level" pandemic in the U.S. could result in 89,000 to 207,000 deaths, between 314,000 and 734,000 hospitalizations, 18 to 42 million outpatient visits, and another 20 to 47 million people being sick if 15 percent to 35 percent of the U.S. population develops influenza in a pandemic. The associated economic impact in our country alone could range between $71.3 and $166.5 billion. A more severe pandemic, as happened in 1918, could lead to much greater damage.

There are several important points about influenza and pandemic influenza.

- A pandemic could occur anytime during the year and could last much longer than inter-pandemic influenza, with waves of infection during the pandemic period.

- At some point in a pandemic, the capacity to intervene and prevent or control transmission of the virus can become extremely difficult because the size of the population that is infected becomes too large.
- Right now, the H5N1 avian influenza strain circulating in Asia among birds is considered the leading candidate to cause the next pandemic. However, it is possible for another influenza virus, and not H5N1, to cause the next pandemic. While we believe some viruses are more likely than others to cause a pandemic, we cannot predict with certainty the risks from specific viruses.
- We often look to history to try and understand how a modern pandemic might affect us and how we might intervene most effectively. However, there have been many changes since the last pandemic in 1968, including changes in population and social structures, medical and technological advances, and the increase in international travel. Some of these changes have increased our ability to handle pandemics, but other changes have made us more vulnerable.
- Because pandemic influenza viruses will emerge in part or wholly from among animal influenza viruses, such as birds, it is critical for human and animal health authorities to coordinate activities such as surveillance and to share relevant information as quickly as possible.

The Current Avian H5N1 Influenza Situation in Asia

For an influenza virus to cause a pandemic, it must (1) be a virus to which there is little or no pre-existing immunity in the human population; (2) be able to cause illness in humans; and (3) have the ability for *sustained* transmission from person to person. So far, the H5N1 virus circulating in Asia meets the first two criteria but has not yet shown the capability for sustained transmission from person to person.

Although the present avian influenza H5N1 strain in Asia does not yet have the capability of sustained person-to-person transmission, at least 100 persons have been infected, largely by having some form of contact with infected poultry, primarily chickens. In addition, a limited number of persons have been infected by very close contact with another infected person, but this type of transmission has not led to sustained transmission or large outbreaks. As of June 17, 2005 the World Health Organization (WHO) had confirmed 107 cases of H5N1 influenza in humans since January 28, 2004, with a case fatality rate of 51 percent. The World Organization for Animal Health (OIE) confirmed, as of June 8, 2005, that H5N1 had been found in animals from nine Asian countries in 2004 and 2005, with especially large outbreaks among animals in Vietnam and Thailand. Millions of domestic birds have been culled in attempts to stop the spread of the virus among animal populations. In addition to poultry, infections among migratory birds may have also been found since 2002.

At this point, the H5N1 strain now appears to be endemic in poultry and other birds in a number of Asian countries. This situation poses a threat to humans because H5N1 from such sources can continue to infect people and because persistence of H5N1 in these populations provides the virus with chances to mutate or reassort its genes with genes from other viral strains and create H5N1 viruses that can transmit easily among people. Recent studies also have found that domesticated ducks can appear healthy but carry and shed the H5N1 strain, allowing the virus to spread invisibly to other species. H5N1 also has been shown to naturally infect mammals, which is a particular concern because this increases the potential for H5N1 viruses to reassort with other influenza strains that already have the ability to spread among humans and other mammals. Studies have documented H5N1 infections of pigs, tigers, and leopards in Asia.

To monitor H5N1 viruses for changes indicating an elevated threat for people, we must continue to strengthen and build effective in-country surveillance, which includes enhancing the training of laboratorians, epidemiologists, veterinarians, and other professionals, and promoting the comprehensive reporting that is essential to monitor H5N1 and other strains of highly pathogenic avian influenza.

Responding to a Pandemic

Although the current situation is very serious, it remains relatively localized to Asia. However this situation could evolve into a pandemic, in which case the entire world's population would be at risk for developing pandemic disease. An

effective response to an influenza pandemic requires highly collaborative planning, implementation, and flexibility in resolving issues at many levels. DHHS is leading the coordination of preparedness efforts through its *Pandemic Influenza Response and Preparedness Plan*, which was released in draft form in August 2004 for public comment and is under revision. In addition, states are either developing pandemic influenza plans or revising existing plans to reflect new information and data. Key elements of these plans include the use of surveillance, infection control, antiviral medications, community containment measures, vaccination procedures, communications, and an ability to sustain essential services in times of widespread illness. To support the federal and state planning efforts, CDC is developing detailed guidance and materials for states and localities, and this guidance will be incorporated into the revised DHHS plan. CDC also is taking a lead role in working with the Advisory Committee on Immunization Practices and the National Vaccine Advisory Committee to recommend prioritized target groups for use of antiviral medications and vaccines during a pandemic when supplies are limited.

In the earliest pandemic stages, isolation precautions for persons who are ill and quarantine for persons exposed probably will be needed to try and limit the spread of pandemic influenza and to obtain as much time as possible for producing supplies of a pandemic vaccine. These control measures will require interventions such as the evaluation of ill travelers. Certain steps have been taken or will be taken to facilitate such efforts. On April 1, 2005, the President

amended Executive Order 13295, adding influenza caused by novel or reemergent influenza viruses that are causing, or have the potential to cause, a pandemic to the list of quarantinable diseases. CDC will implement travel notices to minimize the potential for infection to rapidly spread. Recently, CDC expanded the number and capacity of its quarantine stations at major ports of entry into the U.S. As with any quarantine, such activities need to be undertaken judiciously to minimize adverse effects on civil liberties.

Vaccination is the best overall, long-term strategy to reduce disease from inter-pandemic influenza outbreaks and pandemics. Antiviral medications, which can be used to prevent influenza and in some instances to treat influenza, provide another line of defense. These types of measures, together with those such as isolation of ill persons and quarantine of healthy exposed persons, help form a comprehensive preparedness approach both to address inter-pandemic influenza and to lay the foundation for responding to pandemic influenza.

Surveillance

Surveillance is critical for detecting and monitoring all infectious disease threats. Because early detection means having more time to respond, it is critical for the U.S. to work with domestic and global partners to expand and strengthen the scope of early-warning surveillance activities used to detect the next pandemic. We do not know how long it will take for pandemic disease in another country to spread to the U.S., but it could be a matter of days to months. And yet, months

of time, at best, will be needed to develop, produce, test, and administer vaccine to the entire U.S. population. Vaccine will be in short supply at the start of the pandemic and under the most favorable conditions, many will have become ill or died by the time the first dose of vaccine would be available to be given to the first person in this country. Global surveillance will also be used to monitor ongoing changes in a pandemic virus and thus allow us to know when the vaccine should be updated.

The outbreaks of avian influenza in Asia have highlighted several gaps in global disease surveillance that the U.S. must help address to improve our ability to prepare for an influenza pandemic. These limitations include (1) a lack of infrastructure in many countries for in-country surveillance networks; (2) the need for better training of laboratory, epidemiologic, and veterinary staff; and, (3) the resolution of longstanding obstacles to rapid and open sharing of surveillance information, specimens, and viruses among agriculture and human health authorities in affected countries and the international community.

In the past year, CDC and DHHS have made significant progress toward enhancing surveillance in Southeast Asia. However, this initiative needs to continue at both national and international levels if we are to sustain our progress, expand geographic coverage, and develop an adequate capacity to conduct effective surveillance. These efforts at building international as well as domestic surveillance are essential for detecting new influenza virus variants

earlier and making informed vaccine decisions for inter-pandemic influenza. With the ever-present threat of the emergence of a new pandemic strain, we need to know what is happening in commercial poultry farms and the family backyard flocks of Southeast Asia, as well as elsewhere throughout the world.

Recently, Congress passed and the President signed an FY 2005 Emergency Supplemental Appropriations Act for Defense, the Global War on Terror, and Tsunami Relief, which included $25 million in international assistance funds to prevent and control the spread of avian influenza in Asia. These funds will support disease surveillance among humans, laboratories, and training on avian influenza laboratory and field techniques in Asia. They are being provided both to the region of Southeast Asia and to six specific nations where human and/or animal disease is greatest. Funding will support the planning and preparedness needed to enable each country to carry out a rapid response in a more organized manner. National long-term planning is also necessary for these countries; therefore they must also strategically apply to non-governmental organizations for additional funds to complete their preparedness efforts. Funds are also being provided for three countries, Cambodia, Laos, and Vietnam, to conduct active case detection of human disease, and additionally to Burma, China, and Indonesia for detection of animal disease. With respect to Burma, any avian flu assistance activities would be channeled through international non-governmental organizations or be conducted by international health organizations and not through the Burmese government. We will be happy to brief Congress on the

specific activities that will involve Burma. Improved laboratories, including addressing biosafety for animal and human specimens will be the initial focus. Better in-country communications will be developed to assist these populations to taking steps to prevent infection and disease. Direct assistance to Vietnam will provide technical help for the safe development of an H5N1 vaccine. Finally, rapid response teams for Vietnam, Cambodia, and Laos will be organized and trained to respond to a crisis by identifying disease and instituting quarantine, isolation, and any other control measures that are necessary. These teams will be supplied with materials to be stockpiled in Southeast Asia, so that they will be equipped with proper personal protective equipment when they conduct case investigations.

On the domestic side, during the past year, CDC has considerably improved surveillance in this country by working with the Council for State and Territorial Epidemiologists (CSTE) to make pediatric deaths associated with laboratory confirmed influenza nationally notifiable, and by implementing hospital-based surveillance for influenza in children at selected sites. CDC will continue to work with CSTE to make all laboratory confirmed influenza hospitalizations notifiable. Since 2003, we have issued interim guidelines to states and hospitals for enhanced surveillance to identify potential H5N1 infections among travelers from affected countries, and these enhancements continue. CDC also has been holding special laboratory training courses to teach state laboratory staff how to

use molecular techniques to detect avian influenza. CDC has trained professionals from all 48 states that desired training.

In addition, we are working to: (1) ensure that states have sufficient epidemiologic and laboratory capacity both to identify novel viruses throughout the year and to sustain surveillance during a pandemic; (2) improve reporting systems so that information needed to make public health decisions is available quickly; (3) enhance systems for identifying and reporting severe cases of influenza; (4) develop population-based surveillance among adults hospitalized with influenza; and, (5) enhance monitoring of resistance to current antiviral drugs, to guide policy for use of scarce antiviral drugs.

Managing the Vaccine Supply

During an influenza pandemic, the presence of influenza vaccine manufacturing facilities in the U.S. will be critically important. The pandemic influenza vaccines produced in other countries are unlikely to be available to the U.S. market, because those governments have the power to prohibit export of the vaccines produced in their countries until their domestic needs are met. The U.S. vaccine supply would be particularly fragile; only one of three influenza vaccine manufacturers selling vaccine in the U.S. market makes its vaccine entirely in the U.S.

In the U.S., public demand for influenza vaccine varies on a yearly basis, but having a steadily increasing demand would provide companies with a reliable, growing market that would be an incentive to increase production. In FY 2006, DHHS and CDC have provided $40 million in new funds for purchasing influenza vaccine for the pediatric stockpile to protect against annual outbreaks of influenza, and $30 million for contracts to expand the production of bulk single-strain influenza vaccine for use if needed during annual influenza seasons or possibly in a pandemic situation. In addition, the President is requesting $120 million in FY 2006, an increase of $21 million, to encourage greater production capacity that will enhance the U.S.-based vaccine manufacturing surge capacity to help prepare for a pandemic and further guard against annual shortages.

DHHS also appreciates the inclusion of $58 million in the FY 2005 Emergency Supplemental to procure additional influenza countermeasures for the CDC Strategic National Stockpile (SNS) in FY 2005. At present, the H5N1 viruses isolated from people in Asia during the past two years appear resistant to one class of antiviral drugs but sensitive to oseltamivir (Tamiflu). Accordingly, the SNS has stockpiled enough oseltamivir (Tamiflu) capsules to treat approximately 2.26 million adults and oseltamivir (Tamiflu) suspension to treat nearly 110,000 children. With the increased funding, CDC plans to purchase an additional 2 million regimens of oseltamivir. In addition, SNS funds have been used to purchase approximately 2 million bulk doses of unfinished, unfilled H5N1

vaccine. This vaccine has not yet been formulated into vials, nor is the vaccine licensed. Clinical testing to determine dosage and schedule for this vaccine began in April 2005 with funding from the National Institutes of Health. Additionally, DHHS also is supporting the development and testing of potential dose-sparing strategies that potentially could allow a given quantity of vaccine stock for use in more people.

One of the main efforts by CDC is to expand the nation's use of influenza vaccine during inter-pandemic influenza seasons. This increase will help assure that the U.S. is better prepared for a pandemic. Influenza vaccine demand drives influenza vaccine supply. Therefore, if we can increase annual vaccination efforts, we will increase annual production efforts, which help strengthen our capacity for vaccine production during a pandemic. Discussions are under way to review the studies that would be needed to consider broadening recommendations for influenza vaccination. CDC also is developing strategies to increase influenza vaccine demand and access by persons who are currently recommended to receive vaccine each year. For example, according to a 2003 Institute of Medicine report, there are approximately 8.2 million uninsured adults 18-64 years with high-risk conditions warranting vaccination against influenza. If such persons receive influenza vaccine, it will help to increase annual demand for vaccine, because one of the best predictors of being vaccinated is having been vaccinated in a previous season. This increase in annual demand will lead

to increased production capacity, and thereby increase vaccine supply both annually and during a pandemic.

Additionally, for planning purposes, CDC has identified influenza vaccine supply scenarios that may occur in future influenza seasons. These scenarios range from worst-case to best-case situations and are an important part of CDC planning efforts. We are preparing recommendations, plans, and communication messages for each of these possible situations.

Conclusion

Although the present avian influenza H5N1 strain in Southeast Asia does not yet have the capability of sustained person-to-person transmission, we are concerned that it could develop this capacity. CDC is closely monitoring the situation in collaboration with the World Health Organization and the affected countries. CDC is using its extensive network of partnerships with other federal agencies, provider groups, non-profit organizations, vaccine and antiviral manufacturers and distributors, and state and local health departments to enhance pandemic influenza planning. Our responses to the annual domestic influenza seasons provide the core foundation for how the nation will face and address pandemic influenza.

Thank you for the opportunity to share this information with you. I am happy to answer any questions.